Association of Cutibacterium avidum Colonization in the Groin With Obesity: A Potential Risk Factor for Hip Periprosthetic Joint Infection

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Abstract: Background An increase in the incidence of hip periprosthetic joint infections (PJIs) caused by Cutibacterium avidum has recently been detected after implantation of hip arthroplasties with an anterior surgical approach. We raised the question of whether skin colonization with C. avidum differs between the anterior and the lateral thigh as areas of surgical incision fields. Methods Between February and June 2017, we analyzed skin scrapings from the groin and the anterior and lateral thigh in all patients undergoing a primary hip arthroplasty. We anaerobically cultured plated swabs for Cutibacterium spp. for at least 7 days. Univariate logistic regression analysis was used to explore associations between body mass index (BMI) and colonization rate at different sites. Results Twenty-one of 65 patients (32.3%) were colonized with C. avidum at any side, mainly at the groin (n=16, 24.6%), which was significantly higher than at the anterior (n=5, 7.7%, P= 0.009) or lateral (n=6, 9.2%) thigh (P=0.019). Patients colonized with C. avidum did not differ in age or sex compared to non-colonized patients, but BMI was significantly higher (30.1 kg/m2 and 25.6 kg/m2, respectively, P=0.019). Furthermore, increased BMI was associated with colonization at the groin (odds ratio per unit BMI increase: 1.15, 95% confidence interval: 1.03-1.29, P=0.014). Conclusions The groin, rather than the anterior thigh, showed colonization for C. avidum in obese patients. Further studies are needed to evaluate current skin disinfection and draping protocols for hip arthroplasty surgeries, in particular in obese patients.

DOI: https://doi.org/10.1093/cid/ciy379

Other titles: Working Title : Cutibacterium avidum Colonization in the Groin is Associated with Obesity: A Potential Risk Factor for Hip Periprosthetic Joint Infection (PJI)

Cutibacterium avidum colonization in the groin is associated with obesity: a potential risk factor for hip periprosthetic joint infection (PJI)

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Summary

We found that 21 out of 65 patients (32.3%) undergoing a hip arthroplasty surgery were colonized with *Cutibacterium avidum* in the hip area, mainly at the groin as a potential risk factor for hip periprosthetic joint infections.

Abstract

Background. An increase in the incidence of hip periprosthetic joint infections (PJIs) caused by *Cutibacterium avidum* has recently been detected after implantation of hip arthroplasties with an anterior surgical approach. We raised the question of whether skin colonization with *C. avidum* differs between the anterior and the lateral thigh as areas of surgical incision fields.

Methods. Between February and June 2017, we analyzed skin scrapings from the groin and the anterior and lateral thigh in all patients undergoing a primary hip arthroplasty. We anaerobically cultured plated swabs for *Cutibacterium* spp. for at least 7 days. Univariate logistic regression analysis was used to explore associations between body mass index (BMI) and colonization rate at different sites.

Results. Twenty-one of 65 patients (32.3%) were colonized with *C. avidum* at any side, mainly at the groin (n=16, 24.6%), which was significantly higher than at the anterior (n=5, 7.7%, *P*= 0.009) or lateral (n=6, 9.2%) thigh (*P*=0.019). Patients colonized with *C. avidum* did not differ in age or sex compared to non-colonized patients, but BMI was significantly higher (30.1 kg/m^2 and 25.6 kg/m^2, respectively, *P*=0.019). Furthermore, increased BMI was associated with colonization at the groin (odds ratio per unit BMI increase: 1.15, 95% confidence interval: 1.03-1.29, *P*=0.014).

Conclusions. The groin, rather than the anterior thigh, showed colonization for *C. avidum* in obese patients. Further studies are needed to evaluate current skin

disinfection and draping protocols for hip arthroplasty surgeries, in particular in obese patients.

Keywords: *Propionibacterium avidum*, *Cutibacterium avidum*, periprosthetic joint infection (PJI), hip, colonization, anterior surgical approach

Introduction

Microorganisms of the patient's skin may cause postoperative infections after implantation of arthroplasties. The most commonly isolated bacteria are staphylococci, streptococci, enterococci, gram-negative bacteria, and anaerobes, such as *Cutibacterium* spp. (formerly known as *Propionibacterium* spp.). [1, 2]. *Cutibacterium avidum* is a gram-positive anaerobic rod [3] belonging to the cutaneous group of human cutibacteria with preferential colonization of sweat glands in moist areas, such as the groin [4]. Only a few *C. avidum* infections of soft tissues, bones, or joints have been described in the literature [5-10]. In a recent publication, we showed that the skin commensal *C. avidum* was increasingly isolated as the causing pathogen of hip periprosthetic joint infection (PJI) at our institution [11]. Regarding our epidemiological data of *C. avidum* hip PJI over time, we speculated that the increased rate of these infections was associated with the recent change from a lateral transgluteal to an anterior surgical approach in our hospital (Figure 1), because the incision of the anterior approach has a closer relation to the groin. In addition, we asked if obese patients were at risk for colonization of *C. avidum* in skin folds of the groin, facilitating bacterial entry into the nearby incisions.

To address these questions, we conducted a prospective study to determine how often patients undergoing primary total hip arthroplasties were colonized with cutaneous cutibacteria at different sites in the hip region. Furthermore, we investigated whether colonization with *Cutibacterium* sp. was associated with sex, BMI, site of skin colonization in the hip or groin, or any other *Cutibacterium* spp.

Materials and Methods

Patients and study design

We conducted a prospective analysis at the Department of Orthopedics of the University Hospital Balgrist from February 2017 to June 2017 to identify skin colonization with *Cutibacterium* spp. in the hip area at time of primary implantation of a hip arthroplasty. Clinical data of included patients (age, sex, gender, BMI) were retrieved from the hospital clinical information system. The cantonal ethics committee of Zurich, Switzerland, approved the study protocol (BASEC-Nr 2016-01017).

Routine disinfection before hip arthroplasty surgery with an anterior surgical incision

Antiseptic disinfection of the skin with a povidone-iodine/alcohol solution (Betaseptic®, Mundipharma, Limburg, Germany) was routinely performed under laminar flow (repeated three times). The disinfection covered the skin area from the iliac crest to the lateral knee, medially up to the pubis. Once the disinfectant had dried, four sterile drapes were used to cover the area around the surgical field (proximal: 5 cm above the anterior superior iliac spine, distal: 10 cm above the knee, medial: 5 cm medial of the anterior superior iliac spine, and lateral: 5 cm lateral of the greater trochanter). The surgical incision was marked from the anterior superior iliac spine in the direction of the lateral patella, with a size of 8-10 cm. Finally, a sterile adhesive surgical iodine film (Steri-DrapeTM IobanTM 2, 3M Health Care) was applied to cover the entire area, including the sterile drapes (Supplemental Figure 1).

Specimen collection

In the operating room, prior to the time of surgical disinfection of the patient, microbiological samples from the skin of three different sites were taken of the

contralateral site of the operating hip. We collected the samples by scraping the skin with sterile blades [12]. Skin scrapings were removed from blades and entered into ESwab culture swabs (Copan, Breschia, Italy). The swabs were sent to the Institute of Medical Microbiology of the University of Zurich in Zurich, Switzerland, for bacterial culture.

The contralateral hip was chosen to avoid superficial skin lesions in the area of the incision with the potential risk of postoperative wound healing problems. Two sites were chosen according to the anterior and lateral (transgluteal) surgical incision approaches (Figure 1) in hip arthroplasties: site A (labeled as “anterior”) above the muscle belly of tensor fascia latae, and site B (labeled as “lateral”) at the level of the greater trochanter. The groin was taken as the control site and scraped midway between the symphysis and the anterior superior iliac spines.

Bacteriology

Sample swabs were streaked out onto Columbia sheep blood agar plate without antibiotics (bioMérieux, Mary-l’Etoile, France), colistin-nalidixic acid (CNA) blood agar (bioMérieux) plate for aerobic cultivation, and a Brucella plate (in-house 10% sheep blood agar (Becton Dickinson, Heidelberg, Germany) plates with hemin and vitamin K1 (SigmaAldrich-Merk, Buchs, Switzerland) for anaerobic cultivation using GENbag (bioMérieux). All three plates were incubated for at least 7 days at 37°C. The range of incubation varied from 7 to 14 days. Any suspicious colony for *Cutibacterium* sp. was further investigated by gram stain and CAMP test for enhanced hemolysis to distinguish *C. avidum* from other *Cutibacterium* spp. [13]. Gram-positive and CAMP-positive bacilli were finally identified using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) using a

Bruker MALDI Biotyper (BD) in combination with research-use-only (RUO) versions of the MALDI Biotyper software package (version 3.0) and the reference database V.3.3.1.0 (4613 entries) or later database versions.

Statistical analysis

Categorical data were tested for differences using Fisher's exact or chi-squared tests, as appropriate, whereas continuous variables were tested using Wilcoxon rank sum tests. Univariate logistic regression analysis was used to explore associations between BMI and *C. avidum* colonization at different sites. Data were analyzed using Stata® version 14.2 (Stata Corporation, College Station, TX). Two-tailed P-values <0.05 were considered statistically significant.

Results

We included 65 patients with a primary hip arthroplasty surgery. The median age of these patients at time of surgery was 65 years (range 24 – 92 years) (Table 1). Approximately half of them were female (n=34, 52.3%), and the median BMI (range) was 26.2 (15.5-40.1) kg/m^2. None of the 65 patients developed surgical site infections according to CDC criteria [14, 15] within six to 12 months.

In general, we found hip colonization with *Cutibacterium* sp. in 44 out of 65 patients (67.7%). Of these 44 patients, 22 (50%) patients were colonized with *C. acnes* only, 15 (34.1%) with *C. avidum* only, and seven patients (15.9%) were colonized with both *C. acnes* and *C. avidum* (n=6), and *C. acnes* and C. granulosum (n=1), respectively (Suppl. Table 1).

Twenty-one out of 44 (47.7%) colonized patients were colonized at only one site, whereas 23 (52.3%) patients were colonized at two or all sites. The groin and lateral sites were more likely to be colonized with *Cutibacterium* spp. (29 out of 65

(44.6%) and 28 (43.1%) patients, respectively) than the anterior site (16, 24.6%) (*P*=0.032).

Colonization rate and risk factors associated with Cutibacterium avidum

Among 65 patients, 21 (32.3%) were colonized with *C. avidum* (15 monocolonized, six co-colonized with *P. acnes*). Colonization in the groin with *C. avidum* (16 out of 65 patients, 24.6%) was significantly more prevalent than colonization of the anterior (n=5, 7.7%, p=0.009) or lateral (n=6, 9.2%, p=0.019) sites (anterior or lateral, 10 out of 65, 15.4%; *P*=0.103).

There was no significant difference in the incidence of *C. avidum* colonization compared to *C. acnes* or *C. granulosum* between the different sites *(Supp. Figure 2*).

Patients colonized with *C. avidum* did not differ in age or sex (Table 1) compared to other patients. However, BMI was significantly higher in patients colonized with *C. avidum* (*P*=0.019). We found no associations with sex, age, BMI, or localization (data not shown) for *C. acnes* and *C. granulosum*.

In logistic regression analysis, we found that the colonization rate in the groin was associated with higher BMI (odds ratio (OR) per unit increase in BMI 1.15, 95% confidence interval (CI) 1.03-1.29, *P*=0.014). In contrast, there was no association between BMI and *C. avidum* colonization rates at the anterior and lateral sites (anterior site: OR 1.08, 95% CI 0.91-1.27, lateral site: OR 1.15 95% CI 0.98-1.36).

Discussion

We found an increased rate of skin colonization of *C. avidum* in the groin compared to the anterior or lateral thigh. We also demonstrated that obesity was associated with the growth of *C. avidum* at the inguinal site.

Our study finding of lower rates of *C. avidum* colonization at the anterior site compared to the skin in the groin does not directly explain the previously published observation of increased *C. avidum* PJIs after changing the surgical incision approach from lateral to anterior in 2006. However, the high colonization rate at the inguinal site near the anterior surgical approach implicates a potential mechanism for wound contamination during surgery. The lateral transgluteal approach has a greater anatomical distance from the potential reservoir of *C. avidum* in the groin (Figure 1). Further studies are needed to evaluate current skin disinfection protocols (Supplemental Figure 1) to analyze whether they has to be adjusted for reducing colonization rates of *C. avidum*. Moreover, an additional draping with a sterile adhesive film might be important to maintain the integrity of the border of the drapes at the groin site in order to avoid becoming loose or permeable for bacteria during surgery.

In general, we found a *C. avidum* colonization rate of 32.3% in the surgical field of hip arthroplasties. Thus far, skin colonization has been mainly described with *C. acnes* but not *C. avidum,* which reflects the current knowledge of mainly *C. acnes* PJIs [3, 16-18] and only three publications so far describing *C. avidum* PJIs [11, 19-21]. Furthermore, skin microbiome data showed skin colonization of *C. acnes* but not of *C. avidum*. We interpret this finding as low abundance of *C. avidum* compared to *C. acnes* with only a few sequenced *C. avidum* strains available at the National Center for Biotechnology Information; however, it could also be due to the swabs and biopsies taken at different locations [12]. Although *C. acnes* and *C. avidum* belong to the same genus, they prefer different skin conditions. *C. acnes* exists in sebaceous glands, whereas *C. avidum* exists in eccrine glands in wet body regions, such as the groin or skin folds [13].

We did not find any other study which shows clinical and microbiological data of hip-colonized patients with *Cutibacterium* sp. We found a similar high rate of skin colonization with *C. avidum* of 32.3% compared to *Staphylococcus aureus* as described between 30 and 50% in the literature [22-25]. In contrast, PJIs caused by *C. avidum* infections are rare, while *S. aureus* dominates the microbiological pathology of PJIs [2]. This contradicting study finding can be rationalized by our differing collection method; we obtained our bacterial culture samples via skin scraping. This method might be superior to skin swabbing for the detection of *Cutibacterium* sp. in the deeper layers of the skin.

Other than obesity, we could not find an association of sex or age with rates of *C. avidum* skin colonization. Our study finding that groin colonization with *C. avidum* is associated with obesity is novel and may be clinically relevant. However, the findings of our single study with only a small number of patients need to be validated in a larger sample. Also, there is need to assess and control for other potential and modifiable confounders that may also be associated with obesity, colonization or both, such as the frequency and type of bathing, use of garments, disruption of the skin microbiome related to recent antibiotic use, weather conditions or season of the year. Prior antibiotic use may thereby be of particular interest, as it was shown that antibiotics may disrupt the skin microbiome and increase the risk of overgrowth with certain bacteria [26]. In addition to the reproducibility of our findings in larger samples of both surgical and non-surgical patients, also the sensitivity of our method of obtaining specimens needs validation. It has been previously shown that a single swab may not be sufficient to assess for *S. aureus* colonization at various body sites [27] and this may also hold true for *Cutibacterium* spp. Furthermore, we did not

assess for the relative quantities of bacteria at the different body sites, which may be relevant with regard to surgical site infection risk [28].

We cannot make a statement about the risk for *C. avidum* PJI in colonized patients since we only have a follow-up of 6 to 12 months after primary hip arthroplasty in 21 colonized patients. In general, the anterior approach is not seen as a risk factor for infections [29]. However, obesity, defined as an elevated BMI, is a known general risk factor for PJIs [29-31]. Our finding of increased *C. avidum* recovery from the groin site of moist skin folds in obese patients could also be a mechanism for pathogens other than *Cutibacterium* sp.

Taken together, *C. avidum* colonization at the groin in obese patients may be a potential risk factor for contamination of the surgical field by using the anterior surgical approach in hip arthroplasty but has to be validated. Further studies are needed to evaluate the efficacy of current skin disinfection protocols. Multicenter studies should explore whether a different skin disinfection will reduce *C. avidum* PJIs.

Acknowledgments.

We thank Susanne Blasowitsch of the Institute of Medical Microbiology of the University of Zurich for expert help and assistance.

Conflicts of Interest

Dr. Kuster received travel accommodations/expenses form Gilead, Astellas, and Ecolab. All authors declare no conflicts.

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Tables and Figures

Table 1. Clinical characteristics of 65 patients undergoing a primary total hip arthroplasty (colonization data according to age, sex, and BMI).

Characteristics	**Total (%)** **n=65**	**Colonized with *Cutibacterium* sp. (%), n=44**	**Not colonized with *Cutibacterium* sp. (%), N=21**	**P-value**	**Colonized with *C. avidum* (%) n=21**	**Not colonized with *C. avidum* N=44**	**P-value**
Median age (range), years	65 (24-92)	64 (24-92)	68 (42-90)	0.28	67 (24-89)	62 (25-92)	0.53
Female, n (%)	34 (52.3)	21 (47.7)	13 (61.9)	0.30	13 (61.9)	21 (47.7%)	0.30
BMI (kg/m^2), median (range)	26.2 (15.5-40.1)	26.8 (18.9-40.1)	25.5 (15.5-34.6)	0.05	30.1 (18.9-37.5)	25.6 (15.5-40.1)	0.019
Low weight (<18.5), n (%)	1 (1.5)	0 (0)	1 (4.8)		0 (0)	1 (2.3)	
Normal weight (18.5-25), n (%)	24 (36.9)	15 (34.1)	9 (42.9)		6 (28.6)	18 (40.9)	
Pre-obesity (25-30), n (%)	21 (32.3)	14 (31.8)	7 (33.3)	0.28	4 (19.1)	17 (38.6)	0.021
Obesity grade 1 (>30), n (%)	11 (16.9)	7 (15.9)	4 (19.1)		5 (23.8)	6 (13.6)	
Obesity grade 2 (>35), n (%)	7 (10.8)	7 (15.9)	0 (0)		6 (28.6)	1 (2.3)	
Obesity grade 3 (>40), n (%)	1 (1.5)	1 (2.3)	0 (0)		0 (0)	1 (2.3)	

Figure legends

Figure 1. Specimen collection at different sites of the hip region without skin disinfection.

Angular lateral view of the hip in panel a: Site 1 = groin, scraped midway between the symphysis (A) and the anterior superior iliac spine (B), site 2 = anterior, scraped above the muscle belly of tensor fascia latae (C), site 3 = lateral, scraped at the level of the greater trochanter (D).

Transversal section in panel b: Anterior and lateral (transgluteal) surgical incision approach in hip arthroplasty. S, Musculus sartorius; T, Musculus tensor fascia latae; R, Musculus rectus femoris; Med, Musculus abductor medius.